Exhibit D

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF WEST VIRGINIA
AT CHARLESTON

IN RE: ETHICON, INC., PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LITIGATION **THIS DOCUMENT RELATES TO WAVE 1 /TVT-S CASES**	**Master File No. 2:12-MD-02327** **JOSEPH R. GOODWIN** **U.S. DISTRICT JUDGE**

RULE 26 EXPERT REPORT OF ANNE HOLLAND WILSON, MBA

I. QUALIFICATIONS

As a Biomedical Engineer and Quality Assurance Consultant, I focus exclusively on medical devices. My work experience includes extensive experience with permanently implantable devices, as well as reusable devices and disposable devices. My areas of expertise include risk management for medical devices, as well as design controls, quality system development, auditing, and manufacturing process optimization.

I received a Bachelor of Science in Biomedical Engineering from Vanderbilt University in 1985, and a Master of Business Administration from the University of Colorado in 1991.

I currently hold certifications as a Certified Quality Auditor, Certified Quality Engineer, and Certified Quality Manager through the American Society for Quality, a Quality System Lead Auditor through Exemplar Global and as Registered Quality Assurance Professional in Good Laboratory Practice through the Society of Quality Assurance. I am a Senior Member and served as Chair of the Austin Section of the American Society for Quality in 2004-2005. In addition to the American Society for Quality, I am a member of the American Society for the Advancement of Medical Instrumentation, Regulatory Affairs Professional Society, and the Society of Quality Assurance. I have also guest lectured at universities and industry seminars on topics such as design controls, risk management and process validation for medical devices.

In 2000, I founded QA Consulting, Inc. where I continue to serve as CEO. I consult with medical device manufacturers to develop and implement compliant solutions for their quality practices. I have completed 100+ supply chain/internal audits to U.S and International Standards. While the 510(k) process is not part of this report, I have been involved in over 30 510(k) applications and am familiar with the requirements relating to FDA clearance of a medical device. The process described herein is not part of the 510(k) process, but instead, part of the Industry standards that medical device companies must follow in designing a safe device for the lifetime of that product.

Prior to creating my company, I worked as a Senior Manufacturing Engineer, QA Manager, and Senior Quality Assurance Engineer over the course of 6 years with Sulzer Carbomedics of Austin, TX. Prior to those positions, I served as Project Manager and Design Assurance Engineer with Ohmeda Monitoring, Quality Assurance Project Engineer with Cobe BCT, Inc., Quality Assurance Engineer with Fischer Imaging Corporation, and Project Engineer with LA BAC Medical Systems.

My 30 years of experience as a Biomedical Engineer in quality assurance, ranging from design concept and research and development through manufacturing/production and post-market surveillance for Class I, II, and III medical devices has afforded me expert knowledge of medical device industry regulations and standards, including but not limited to Title 21 – Food and Drugs of the Code of Federal Regulations, particularly Section 820, Quality System Regulation, and Section 58, Good Laboratory Practice for Nonclinical Laboratory Studies, as well as ISO Standards 13485, Medical Devices - Quality management systems – Requirements for regulatory purposes, 14971, Medical Devices – Application of risk management to medical devices, and 9001, Quality management systems – Requirements.

My experience, education, and certifications along with a complete list of my publications and presentations are outlined in my Curriculum Vitae attached to this report as Exhibit 1.

II. BACKGROUND

I have been asked to address the design control and risk management processes of Ethicon, Inc., Ethicon Women's Heath and Urology, a Division of Ethicon, Inc., Gynecare, and Johnson & Johnson (collectively referred to as Ethicon) associated with the manufacture of the GYNECARE TVT Secur (TVT-S) System which is a medical device indicated for treatment of stress urinary incontinence (SUI). The TVT-S device is a kit which includes the TVT Secur implant, as well as the inserters, finger pads, and release wires.[1] Ethicon documentation reveals that the polypropylene mesh in the TVT Secur device is laser cut, rather than mechanical cut.[2]

All of my opinions expressed in this Report are offered to a reasonable degree of professional certainty within my field.

In the course of my work on this case, I analyzed, reviewed, and relied upon the following categories of information, listings of which are provided in Exhibit 3: (a) Applicable, standards, and guidance documents; (b) Ethicon documents, including, but not limited to risk management documents, and quality assurance documents; (c) Deposition transcripts of Ethicon employees.

In my profession as a Biomedical Engineer and Quality Assurance Consultant for medical device companies, I routinely analyze medical device manufacturers' risk management processes and identify their strengths and weaknesses. In my profession, I regularly look a medical device companies' design and risk management documents, including design history files and FMEAs, and evaluate whether that documentation complies with industry standards and practices. For example, I routinely use root cause analysis to determine deficiencies in medical device

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[1] *See* Eth.Mesh.00309351.
[2] Eth.Mesh.00309362.

companies' risk assessment processes. This is the same analysis and methodology that I have performed in the course of my work in this case.

III. SUMMARY OF OPINIONS

1. Ethicon's Application Failure Mode Effects Analysis (aFMEA) relied exclusively on use of the Instructions for Use (IFU) and physician training to control risks associated with implantation of the TVT-S.[3] All 32 of the potential failures were to be controlled in this manner. The Risk Assessment Summary Reports[4] which evaluate only the most significant harms also conclude that all harms should be addressed by communicating the risk via the IFU. Relying entirely on the IFU is improper under applicable standards because the TVT-S incorporated an entirely new surgical approach and set of instruments. Ethicon's risk analyses showed substantial risks, but those risks were not addressed according to their own internal standards nor to the relevant international standards. Specifically with respect to the TVT-S, Ethicon was forced to acknowledge that the "Secur clearly is a sling 'unto itself," that much relearning had to occur to gain success,[5] and that neither the IFU nor the training courses were effective in mitigating the risks inherent in the new procedure.[6] Thus, the aFMEAs and Risk Assessment Summary Reports dependence on the IFU was unsound in theory and practice. Feedback from Professor Frazer indicated that "the IFU is fundamentally misleading"[7] thus the learning curve was steep and success rate poor.[8]

2. Design validation is a key element in the design control process. It is performed to ensure that the product that has been designed is capable of meeting the user requirements for the intended use.[9] The initial design validation provided data that reasonably suggested that use of the IFU and training materials were inadequate to achieve successful outcomes. Despite the fact that all but one (12 out of 13) of the surgeons were experienced and they were trained just prior to performing the surgeries, "the sessions resulted in a number of significant observations and issues"[10] including the inability to follow the IFU, release wire disengages prematurely, difficulty removing the inserter and implant pulling out along with the inserter. In my opinion, the design validation did not represent the anticipated use conditions and led to false confidence in the performance of the device in the hands of inexperienced users without the benefit of one on one training by the design team. As pointed out when poor performance was achieved, there were huge complication rates with TVT-S due to training concerns.[11]

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[3] Eth.Mesh.00309424.
[4] Eth.Mesh.1135422 and Eth.Mesh.11335589.
[5] Eth.Mesh. 00647412.
[6] Eth.Mesh. 04048585.
[7] Eth.Mesh.00327060.
[8] Eth.Mesh. 04127331.
[9] ISO 13485:2003 Section 7.3.6.
[10] Eth.Mesh.01592121.
[11] Eth.Mesh.04048516.

IV. RELEVANT STANDARDS FOR MEDICAL DEVICE MANUFACTURERS

A. RELEVANT INTERNATIONAL STANDARDS GOVERNING QUALITY MANAGEMENT SYSTEMS.

There have been Quality Management System (QMS) standards applied to many industries, prior to the development and implementation of industry specific standards. One of the first standards used was MIL-Q-9858A Quality Program Requirements which was issued April 9, 1959. MIL-Q-9858A was an input to the ISO 9000 series of standards, Quality systems: Specifications for design/development, production, installation and servicing, which were originally implemented in 1987. It is apparent that international standards governing the QMS and associated risk management practices for medical devices pre-date the initial design of the TVT-S device. These are industry norms which are <u>not optional</u> to implement. My work in this field with medical device companies involves the application and adherence to these standards. The primary standards applicable at the time of development of the TVT-S are described below.

1. <u>ISO 13485 – MEDICAL DEVICES – QUALITY MANAGEMENT SYSTEMS – REQUIREMENTS FOR REGULATORY PURPOSES</u>

ISO 13485 is an medical device industry standard relating to QMS which defines documentation requirements, management responsibilities, human resources design control, product realization, and measurement analysis and improvement. This standard also defines how a medical device manufacturer should handle complaints and product or system related CAPAs once a manufacturer becomes aware of feedback from any source. ISO 13485 has defined the requirements for proper risk analysis in the medical device industry since 1996. The methods for implementation of risk analysis have been deployed using BS EN 1441 and ISO 14971.

2. <u>ISO 14971 – MEDICAL DEVICES – APPLICATION OF RISK MANAGEMENT TO MEDICAL DEVICES</u>

ISO 14971 is the primary standard in the medical device industry defining how to perform risk management, and remains the guiding standard today. While ISO 13485 states that risk management is necessary for medical device manufacturers, ISO 14971 sets forth an overview of essential steps to perform risk management as shown in Exhibit 2.

ISO 14971 specifically calls for: a risk management plan; risk management procedure; and residual risk evaluation and overall residual risk evaluation. A key concept of the standards and their implementation is:

"It is accepted that the concept of risk has two components:

a) the probability of occurrence of harm;
b) the consequences of that harm, that is how severe it might be."[12]

[12] ISO 14971: 2000.

As shown below, while analysis of a medical device involves multi-disciplinary input, the analysis of the risk posed by the design embodies crucial and basic concepts of patient safety. Key questions must be asked, documented, resolved and reviewed before a medical device design is deemed complete and in compliance with industry standard. To ignore this crucial process is a violation of the design standards.

The initial step in risk management related to medical device design is risk analysis for a specific device and intended use. For the risk management process to function properly, such that the device's design does not harm people, the team performing the analysis requires "expertise in areas such as:

- how the medical device is constructed;
- how the medical device works;
- how the medical device is produced;
- how the medical device is actually used;
- how to apply the risk management process."

B. RISK PLANNING USING FMEA ANALYSIS

The purpose of risk management is to protect people from physical injury or damage to health. Risk planning is an essential starting point for defining risk management activities. The plan is utilized to identify both the applicable device(s) and associated life cycle phase. The risk management team and their authorities are also to be defined in the plan. Although no specific risk acceptability levels are prescribed, each company is required to responsibly define their criteria for acceptability within the plan and ensure that a process is in place to apply and assess risk control measures. The medical benefit after application of risk control measures must outweigh the residual risk. This is classic risk-benefit analysis. Key to this analysis (the "risk") is actual occurrence of patient harm.

In order to effectively plan and implement risk management activities, a cohesive team must be formed with clear roles, responsibilities and communications. Members from design, manufacturing, quality, and post-production all must fully participate to achieve the desired outcome. As a leader of many risk management efforts, it is my experience that for risk management to successfully identify all risks associated with a medical device, it is necessary to have feedback from experts in various fields during the design phase. Additionally, the entire product life cycle must be included in the risk management process. A depiction of the interaction between entities for a functioning design control system is shown in Figure 1 below.

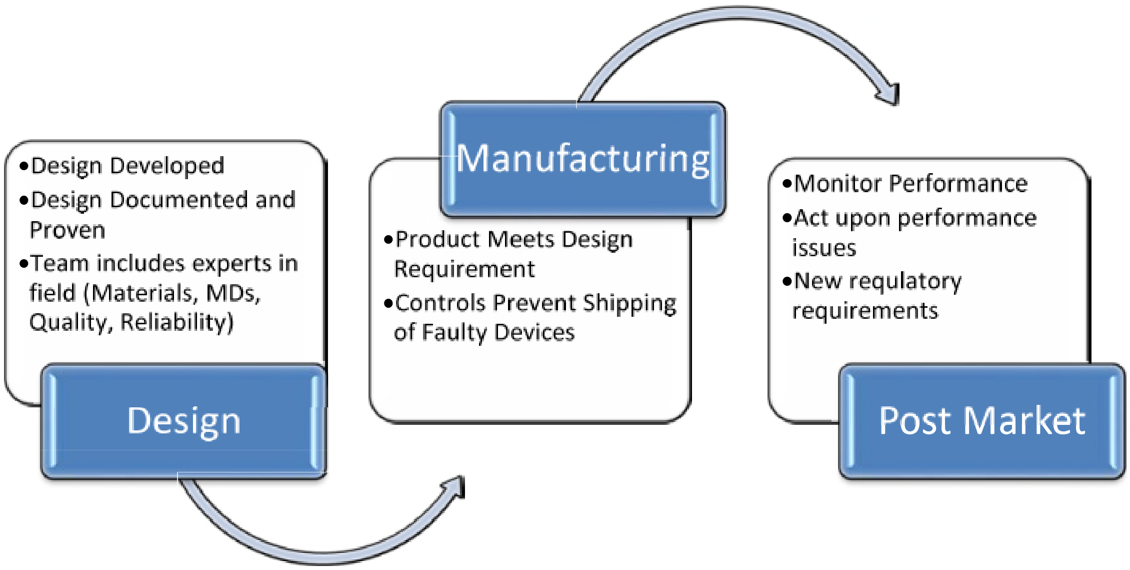

Figure 1: Team Collaboration for Effective Risk Management

There are several tools that may be utilized to implement risk management activities. These include, but are not limited to, fault tree analysis (FTA), failure mode effect analysis (FMEA), and hazard and operability study (HAZOP). In my experience, of all the risk management tools, the FMEA analysis is utilized most frequently for analysis of risk in medical devices.

The FMEA is a risk analysis tool for identifying all possible potential modes of failure in a design.[13] "Failure modes" means the ways, or modes, in which something, such as a medical device, might fail both under intended use and foreseeable misuse conditions.[14] Failures are any errors or defects, especially ones that affect the customer, and can be potential or actual. "Effects analysis" refers to analyzing the consequences of those failures. The FMEA encompasses the identification of the potential causes of failure, an estimate of their severity, the potential frequency, as well as the potential for these failures to be detected. For every risk that is identified, a manufacturer then has a duty to mitigate the risk as far as possible, meaning that they need to reconsider the design of the product so as to eliminate any potential risks to the fullest extent feasible. This is true for all kinds of medical devices. If risk mitigation cannot occur through product design, a manufacturer must attempt to minimize the risk by incorporating protective measures. A protective measure, in the cases of an implant, could be the addition of an accessory to the kit that makes the surgery more precise or reliable such as a guide or tool, or a tool to remove the device in the event of a complication. I have worked with medical device companies that have incorporated such protective measures for implantable devices. The manufacturer may also add a warning about the hazards, and provide training to the product's users. Warnings and training are the least effective means of minimizing risks of a product and should only be used as a last option.

[13] ISO 14971: 2007 Medical devices- Application of risk management to medical devices.
[14] Id.

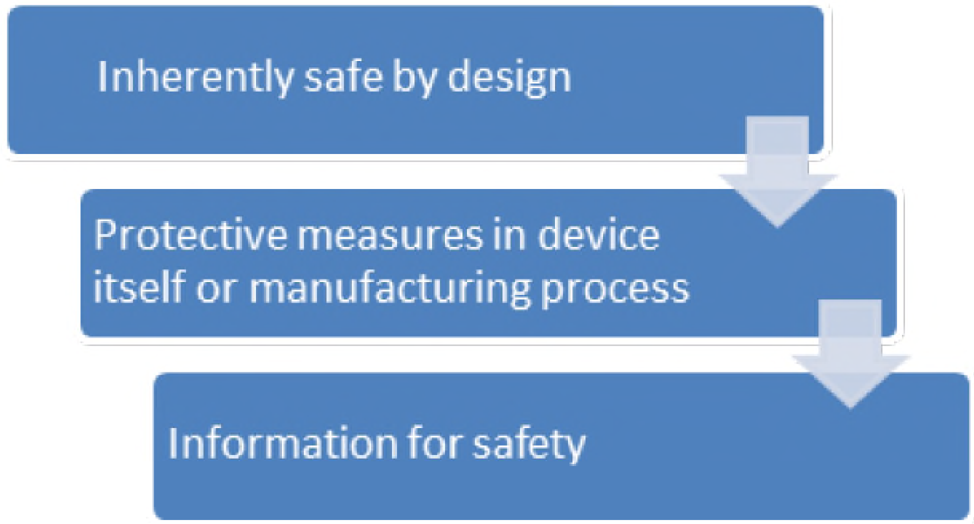

Figure 2: Risk Options[15]

For an FMEA to work, all potential risks must be identified to ensure that the product's design is as robust as possible. If this is not done, the manufacturer cannot ensure that the device will function as intended and the manufacturer cannot ensure the safety of the device in patients.

Traditionally, there are four (4) different types of FMEAs that can be conducted during the risk assessment phase of product development: (1) System (concept) FMEA; (2) Design FMEA (dFMEA); (3) Process FMEA (pFMEA); and (4) Service FMEA (sFMEA).[16] In my experience, manufacturers of non-active permanently implantable medical devices do not conduct sFMEAs because repair and maintenance activities are not anticipated. Instead, an application FMEA (aFMEA) is often conducted in conjunction with the dFMEA to look at potential failures associated with the use and misuse of the product by the end user.[17]

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[15] Id.
[16] Failure Mode and Effect Analysis, FMEA from Theory to Execution, D. H. Stamatis, Second Edition, p.40.
[17] Id.

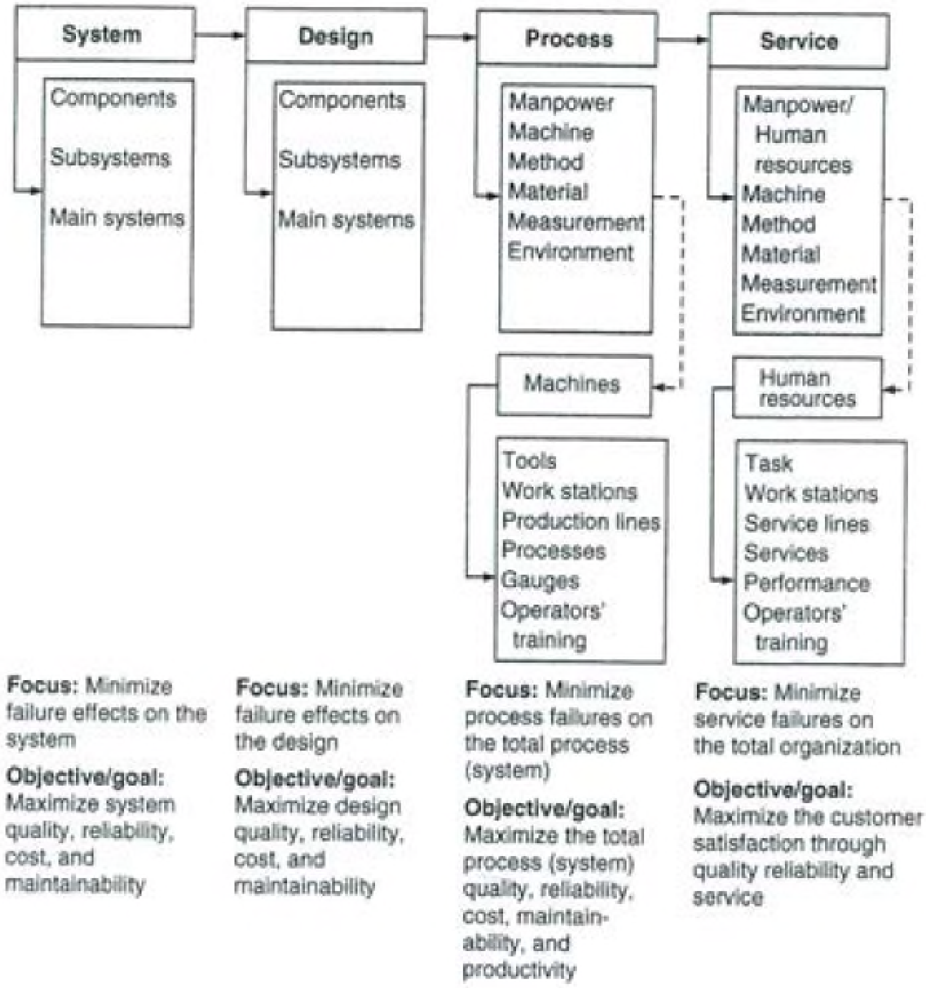

Figure 3: Types of FMEAs[18]

Acknowledging that use of a medical device entails some degree of risk,[19] the dFMEA is conducted during the design phase of product development to ensure any and all product and system related features that could lead to patient harm are identified and designed out of the system to the extent feasible. For product features that could harm a patient, a pFMEA is conducted on the manufacturing process for a new product, and an aFMEA looks at risks associated with the application or a product (such as surgical implant of the device). An FMEA requires the identification of all potential failure modes for a particular product. For each potential failure mode, an estimate is made for its severity (S), or its occurrence rate (O), and its ability to be detected (D).

The "System" FMEA is one of the four (4) types of generally accepted FMEA's. The system FMEA is a predecessor of or may be integrated with the design dFMEA and focuses on failure modes between the system functions (such as the needle, tape and guide) to identify system

[18] Failure Mode and Effect Analysis, FMEA from Theory to Execution, D. H. Stamatis, Second Edition, p.41.
[19] ISO 14971: 2000 and ISO 14971: 2007 Medical devices- Application of risk management to medical devices.

interactions and deficiencies.[20] System level analyses are critical in that they directly relate to the overall application of the system in its intended use environment rather than only constituent parts. A system level FMEA would consider for example, where a device is inserted, the final placement of the device, instrumentation utilized and instructions for use and/or surgical technique. The goal is to identify the risks associated with the entire system itself when used as intended and with reasonably foreseeable misuse[21] by the medical device manufacturer.

C. POST-MARKET PRODUCT ASSESSMENT REQUIRES RISK MANAGEMENT PROCESS INPUTS

The FMEA is considered a living document that must be updated to take into account any additional risks or failure modes that are identified during both the design phase and during the product's lifecycle. After a device is on the market, information is gathered through multiple sources including product complaints and others as illustrated in **Figure 4.** As such, medical device manufacturers are also required to vigilantly assess performance after the product is on the market. This requires risk management process inputs, meaning that the product manufacturer must continue to gather information related to its products and then identify the root cause of the product's failure. The manufacturer is in the best position to gauge what information must be collected. In my experience, the manufacturer of an implantable medical device will not only collect and review patient complaints, but will set up systems staffed with the necessary experts to retrieve the explanted device and analyze it for root cause failure. These concepts are well-recognized industry standards that can be achieved quickly and efficiently. In fact, I have personally been involved in such efforts with implantable medical devices during the course of my career, which involved notifying physicians and patients and retrieving implantable devices to gather root cause failure data. The standards require this basic vigilance when patient safety is at risk, especially in a permanently implantable device.

If, and when, additional or unanticipated risks are identified, the risks must be added to the original FMEA, and the FMEA must be updated to show how the risk was identified, analyzed, and then mitigated. Identification of new risks requires a medical device manufacturer to analyze and, if appropriate, change the design of its product or system so as to eliminate or minimize the risk to patients. To comply with QMS requirements, complaints and other forms of feedback are to be routinely trended using statistical techniques to identify changes in product or service performance that do not occur by chance (i.e., are statistically significant). This process then repeats on a periodic basis and new failure modes are identified and brought to the attention of Executive Management during Management Review, as required by ISO 13485. In short, this means that Management of the medical device manufacturer must follow up on these identified failure modes to ensure that action is taken, either through device changes, updated labeling or field action.

Additionally, each product change should be reviewed to determine if the change could impact the risk assessment of the product. The review of each change for risk applicability should be documented. If properly deployed, the risk management process will create and maintain a robust

[20] Failure Mode and Effect Analysis, D.H. Stamatis, Second Edition, Pg.41.
[21] ISO 14971: 2007 Medical devices- Application of risk management to medical devices.

product design as it will help ensure that the product that is on the market is safe, performs as intended, and that known or knowable risks will be identified, and warned about or mitigated. Figure 4 illustrates a depiction of the after-market process for ensuring design safety. As shown, numerous inputs are monitored, documented and Executive Management takes corrective action where necessary.

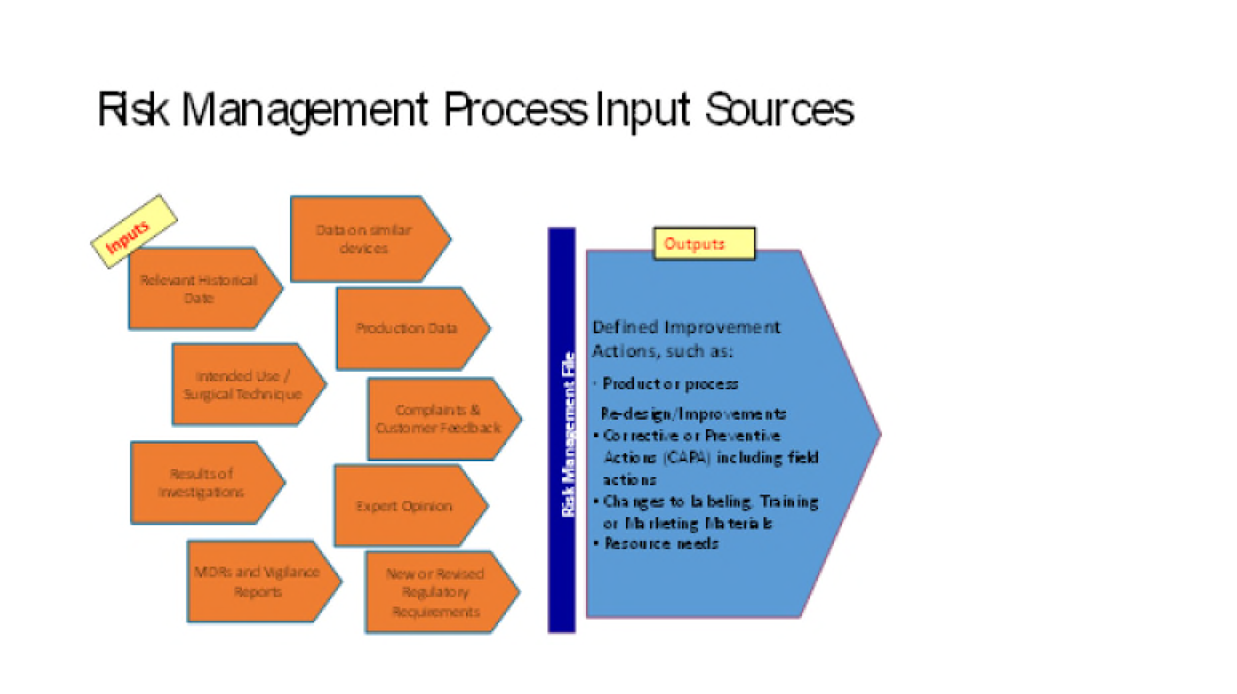

Figure 4: TVT Risk Management Process Input Sources

D. ETHICON'S OWN INTERNAL STANDARDS REGARDING RISK MANAGEMENT

Ethicon's own internal risk assessment documents and witnesses confirm that the risk management process is as I have described it. Dan Smith, Ethicon's Corporate Representative for the design and development of Ethicon's Stress Urinary Incontinence products, acknowledged that Ethicon's internal policies are actually written to comply with the international standards.[22] At Ethicon, the Medical Affairs department was tasked with being the final "approver" of the risk management process.[23] Testimony of Ethicon engineers has confirmed that the FMEA process is intended to capture "all of the potential risks to a patient's health or safety.[24] Dan Smith, Ethicon's Corporate Representative for the design and development of Ethicon's SUI products products acknowledged that Ethicon's risk management tools are supposed to assess known risks.[25]

[22] Deposition of Dan Smith, June 4, 2013, 669:1-6.
[23] Deposition of Bryan Lisa, December 19, 2011, 52:1-6.
[24] Deposition of Scott Ciarocca, March 29, 2012, 97:23-98:21.
[25] Deposition of Dan Smith, May 16, 408:19-21.

Aaron Kirkemo, a past Medical Director at Ethicon, testified that once risks are identified, "you will go ahead and if it is an unanticipated event…you need to go back and try to figure out…mitigation strategies."[26] Ethicon employees have also acknowledged that the FMEA "analysis for each product" "should be documented thoroughly within the company."[27] Moreover, Ethicon Regulatory Affairs Manager Bryan Lisa has acknowledged that it is possible that if a risk can't be designed out or is too severe to just warn about, is it possible that the device may not be sold.[28] Testimony of Ethicon employees has acknowledged that the dFMEA goes beyond physical properties of the product and also "addressed how the product is going to perform after it's been placed in a body or when it's being placed in a body."[29]

Dan Smith, Ethicon's Corporate Representative for the design and development of Ethicon's SUI products, explained at his deposition that during the design and development of a device, Ethicon used the Risk Management Reports as described in PR602-003 in conjunction with the dFMEA, aFMEA, and pFMEA to assess risks associated with the design and use of the device.[30]

There are two (2) primary Ethicon procedures that govern the requirements for implementation of Risk Management[31]:

1) PR602-003 Company Procedure for Medical Device Risk Management Plan [32]

This procedure defines the requirements for risk management activities as well as associated responsibilities. The procedure describes required activities and documentation including: a risk management plan, risk analysis, risk evaluation, overall residual risk review, risk benefit analysis and risk management reports. Once the device is on the market, post production data is to be gathered and compared to the anticipated potential hazards at six month intervals after launch for a minimum of two years.

2) OP650-011 Operating Procedure for Design Failure Modes and Effects Analysis Application (aFMEA) or Design (dFMEA)[33]

This procedure provides step-by-step instructions for evaluation and analyzing risks resulting from potential failure modes. The process is defined by means of a flowchart and associated dialogue on how to perform each step. Severity rankings for identified hazards are to be based on the resulting harm that could occur. Severity rankings are to include the worst-case impact of a failure that can reasonably be expected. A severity ranking scale, occurrence rating table and detection table are included to guide the performance of the process. In accordance with OP650-011 unless a risk priority number RPN exceeds two hundred sixty nine (269) with an associated severity of 9 or 10, which represent almost catastrophic or catastrophic respectively, no action or risk benefit analysis is required. Risks determined to be "As Low as Reasonably Practicable" are

[26] Deposition of Aaron Kirkemo, January 6, 2014, 39:14-40:9.
[27] Deposition of Bryan Lisa, December 19, 2011, 49:9-13.
[28] Deposition of Bryan Lisa, December 19, 2011, 51:8-15.
[29] Deposition of Bryan Lisa, December 19, 2011, 47:18-25.
[30] Deposition of Dan Smith, May 16: 303:11-304:8.
[31] Each of these procedures were revised over time; therefore specific requirements associated with each document depends on the exact date in question.
[32] Eth.Mesh.03742598.
[33] Eth.Mesh.03742864.

not reduced unless found to be practical and cost effective. Furthermore, even if a high level of risk is determined, the risk benefit analysis is not required to be conducted until a later date.

V. PROBLEMS WITH ETHICON'S TVT-S DESIGN CONTROL AND RISK MANAGEMENT PROCESS

In the course of my work in this case, I have reviewed the TVT-S Design History File (DHF). Ethicon Engineer Dan Smith, Ethicon's corporate representative regarding the design and development of the TVT family of products, including TVT-S, identified the complete design history file for the TVT-S product at his 30(b)(6) deposition: "Q. And is this an accurate document that reflects the complete design history files for the TVT family of product? A. It is my understanding that is, yes."[34]

1) Design Control

Design validation is required to be performed in accordance with an approved protocol to ensure that the product is capable of meeting the user requirements for the intended use.[35] Design validation is performed on the final product or product representative thereof under simulated use conditions. The Gynecare TVT Secure System design validation protocol dated September 20th 2005[36] was generated and approved by Ethicon to evaluate the packaging, including the IFU, and the product. The validation utilized un-embalmed female cadavers to represent actual anatomy. A minimum of six physicians who were previously trained on TVT products and who had "different levels of experience with the use of other TVT products"[37] for the treatment of SUI were recruited. Both the "U" (similar to retropubic) and "H" (similar to transobturator) surgical approaches were to be evaluated.

The study included a total of 13 users, all but one were experienced in TVT devices with greater than 2 years of use of the TVT-R and/ or TVT-O devices. All users were trained prior to performing the simulated surgeries using both the IFU and an instructional video of the procedures showing the surgical techniques. Despite the fact that the surgeons were experienced and they were trained just prior to performing the surgeries, "the sessions resulted in a number of significant observations and issues."[38] In fact the objectives of the study were not met and would later be seen as surgical

[34] Deposition Testimony of Dan Smith, June 5, 2013, 861:24-862:2 (discussing exhibit 424). Exhibit 424 from this deposition identifies the TVT Secur DHF as containing the following range of documents: ETH.MESH.00223393-ETH.MESH.00223585; ETH .MESH.00752859- ETH.MESH.00753374; ETH.MESH.00759119-ETH.MESH.00759119;ETH .MESH.00759159- ETH.MESH.00759161; ETH.MESH.01407509- ETH.MESH .01410087;ETH.MESH.01591914- ETH.MESH.01592202;ETH.MESH.01592245- ETH.MESH.01592273; ETH .MESH.01594273- ETH.MESH.01594412;ETH.MESH.01594445- ETH.MESH.01594780; ETH.MESH.02312487-ETH.MESH.02312659;ETH .MESH.06703947- ETH.MESH.06708058;ETH.MESH.06716925-ETH.MESH.06716930;ETH .MESH.06717050- ETH.MESH.06717063;ETH.MESH.06717216-ETH.MESH.06717225;ETH.MESH.06717623- ETH.MESH.06717697;ETH.MESH.06717807-ETH.MESH.06717814;ETH.MESH.06717931- ETH.MESH.06717950;ETH.MESH.06717954-ETH.MESH.06718174.

[35] ISO 13485:2003 Section 7.3.6.

[36] Eth.Mesh.01594589.

[37] Id.

[38] Eth.Mesh.01592121.

complications, complaints and high failure rates.[39] Given that the skilled users had difficulties implanting the device and following the IFU, it is no wonder why inexperienced or surgeons without adequate training had failures.

Several of the difficulties encountered in the validation and thought to be "fixed" by Ethicon were seen later as complaints[40, 41], including:

- Implant pulled out along with the inserter during removal of the device
- Difficulty removing the inserter
- Release wire disengages prematurely
- Loose mesh position after pulling out the inserters- tensioning issues

Furthermore Dr. Mokrycki provided numerous comments regarding improvements to the IFU; however Ethicon deemed them to be "no value added"[42] therefore chose not to incorporate them into the IFU.

The design validation was repeated with six users and the report issued February 2006[43]. Five of the six surgeons were experienced users and with the exception of one user, each placed the device in his or her preferred placement. The results met the acceptance criteria and was accepted as confirmation that the user requirements were achieved. In my opinion, the representation of only one inexperienced user that had personalized training from the device design team, does not represent the user population who would be inexperienced in the placement of the TVT-S mini-sling. This may account for the fact that results in the field did not reflect those documented from the small study group in the laboratory setting.

2) Risk Management

I have reviewed additional internal documentation regarding the design and risk assessment of the TVT-S device, including the dFMEA and the aFMEA. It is my opinion Ethicon's risk management activities did not comply with industry standards or Ethicon's own standards nor did they adequately assess all of the known harms associated with the TVT-S device.

A dFMEA[44] was performed once in November of 2005. From the review of the documentation, the analysis did not fully comply with procedural requirements or industry standards, some of which are described below.

None of the 39 potential failure modes determined to be in as low as reasonably practicable region[45] (ALARP) had any further actions taken to reduce the associated risk, nor was there any indication that options were considered. OP650-011 states the "team should discuss actions that could be taken to further eliminate the potential cause, reduce the frequency with which it could

[39] Eth.Mesh.00647414.
[40] Eth.Mesh.10607158.
[41] Eth.Mesh.00006213.
[42] Eth.Mesh.01592121.
[43] Eth.Mesh.01594695.
[44] Dan Smith Deposition Exhibit T-465.
[45] ISO 14971:2000 Annex E.

occur and/or improve the detection".[46] Five possible corrective actions are proved including improving the current control, redesign of the medical device element or improve the reliability program. Industry guidance states that "any risk should be reduced to the lowest level practicable" bearing in mind the benefits of accepting the risk and the practicability of further reduction. Ethicon did not do this. At the time the TVT-S was being designed, practicability included two components: technical practicability and economic practicability. However, the important concept that appears to have been overlooked is that "major risks should normally be reduced even at considerable cost."[47] In other words, patients should not be put at risk because the cost of the hazard reduction impacts a company's profitability. In fact, the concept of economic consideration in risk reduction has since been removed from the current version of ISO 14971[48] to comply with the Essential Requirements, which is a necessary to obtain approval to sell a device in the EU and CE marking.

A harm is defined a physical injury or damage to the health of people, or damage to property or the environment.[49] In 41 out of the 65 defined potential failure modes defined in the FMEA, harms were not determined. For example, if aseptic technique is breached, an infection could occur. It is likely that if harms were appropriately defined, that the outcome of the dFMEA and associated Overall Residual Risk (ORR) may have increased. If all harms had been included, the ORR may have exceeded 29[50], which would have procedurally required Ethicon to perform additional actions in the form of risk/benefit analysis. Furthermore, the Risk Assessment Summary Reports[51], which only address critical harms concludes that all harms were address by communicating them to the user via the IFU.[52]

Review of the aFMEA[53] resulted in 4 failures that exceeded the 269 RPN threshold and required a risk-benefit analysis: 1) inserter not maintaining contact with pubic ramus during advancement leading to bleeding, bladder perforation or hematoma; 2) inserter not maintaining contact with pubic ramus during advancement leading to bleeding requiring a hematoma; 3) removal of the protective cap prematurely leading to infection; and 4) over tensioning leading to urinary retention/ obstruction. The four failures were evaluated in a risk/benefit analysis completed by David Robinson;[54] he deemed all acceptable based upon comparison to the TVT-R and TVT-O data. However, the acceptance of urinary retention failures, predicated on the design of TVT-R and TVT-O, clearly contradicts the Clinical Evaluation Report equivalence criteria documented by Piet Hinoul MD.[55] That states that " while the TVT Secur has similar intended use and biological characteristics to the GYNECARE™ TVT-R Tension- free Support for incontinence and GYNECARE™ TVT Obturator System Tension- free Support for incontinence, they have not been included in the CER as equivalent to TVT Secur based on the latter's single incision application." In my opinion, a consistent approach was needed to evaluate acceptability of risk and

[46] Eth.Mesh.03742864.
[47] ISO 14971:2000 Annex E.
[48] ISO 14971:2012.
[49] ISO 14971:2000.
[50] Eth.Mesh.03742598.
[51] Eth.Mesh.1135422 and Eth.Mesh.11335589.
[52] Id.
[53] Eth.Mesh.00823549.
[54] Eth.Mesh.08759304.
[55] Eth.Mesh.11335606.

that the data from TVT-R and TVT-O could not appropriately be leveraged to accept the risks associated with introduction of an entirely new and clinically different system.

VI. PROBLEMS WITH ETHICON'S COMPLAINT REPORTING

The failure to carefully consider the implications of relying on training and the IFU when introducing a significantly different product such as the TVT-S mini-sling was unsound. Post–launch risk management activities were summarized in a memo from Gary Borkes,[56] which described that neither the initial post production risk review conducted in November of 2006 nor the second review in Jun of 2007 warranted "substantive changes to TVT-Secur Risks Management documentation (RMR, FMEAs)." The risk management documents were not updated until 2008; even then, only risks associated with the addition of in-office use environment were added.[57] Review of the Risk Management report actually decreased the overall residual risk (ORR) for the TVT-S from a value of 26 to 20[58] despite the known high failure rates[59] and decision to cease marketing the product in Australia. Training issues were not addressed at that time regardless of key opinion leaders (KOLs) voicing concern regarding huge complication rates with TVT-S because of training concerns: the "training is so poor is so many countries."[60]

Post-market surveillance data compiled for January 2010 to April 2013 [61] demonstrated that several of the problems identified in the initial design validation continued to occur including: [62]

- Post-procedure incontinence due to difficulty tensioning
- Implant pulls out with inserter
- Premature separation of mesh from inserter
- Release wire disengages prematurely

These problems, and others, should have been considered, addressed and reduced in the initial design stages to protect patient safety. This includes a lack of a mitigation to address the harms related to the stiffer presentation of laser cut mesh (LCM). This is of particular importance given the evidence that Ethicon personnel did not act on complaint reports until years after they occurred.[63]

VII. CRITICAL RISKS IGNORED BY ETHICON

The failure to properly adhere to the design process without proper checks and balances jeopardizes patient safety. In this case, the data reviewed demonstrates that Ethicon's QMS did not ensure that the proper design controls and risk management processes had addressed several known risks associated with the TVT-S device. Had the QMS's design control and risk

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[56] Eth.Mesh.00823952.
[57] Id.
[58] Id.
[59] Eth.Mesh.02154878.
[60] Eth.Mesh.04048515.
[61] Eth.Mesh.10607158.
[62] Id.
[63] *See e.g.*, Deposition of Lynn Meyer, August 20, 2014, Lynn Meyer deposition at 136:2-138:4; 138:8-143:9; 147:6-148:7.

management processes been properly implemented for the device, the risks should have been addressed and therefore minimized. These known risks and/or failure modes include, but are not limited to:

1) Polypropylene's susceptibility to in vivo degradation;
2) Increased stiffness of LCM;
3) IFU did not warn about TVT-S Risks;
4) Physician problems tensioning the TVT-S device;
5) Physician learning curve with the TVT-S device;
6) The inability to remove the TVT-S device.

1. Polypropylene's susceptibility to in vivo Degradation

Before the launch of the TVT-S device, it was known both in the industry[64] and within Ethicon that the Prolene® material from which the TVT-S is manufactured degrades over time. A series of internal reports on the outcomes associated with implantation of Prolene® sutures in human and canine explant studies were documented from 1983[65] through 1992.[66] It was shown as early as 1983 that cracking occurred and documentation of these studies revealed that "it is obvious that the severity of cracking is related to the implantation time."[67] Additionally, the studies concluded the polypropylene "appears to be degraded in an oxidative fashion."[68] Furthermore, Ethicon scientist Thomas Barbolt testified that it is Ethicon's position that degradation can occur and this was known by Ethicon as early as 1992.[69] Thomas Barbolt acknowledged Ethicon's internal studies have shown that the Prolene mesh is susceptible to degradation.[70] Moreover, several peer-reviewed published articles have reported that polypropylene material may be susceptible to degradation after implantation in the body.[71]

Within the context of Risk Management, it is evident that material degradation was not considered as a hazard which, over time, could lead to mesh embrittlement, cracking and loss of mechanical strength within the patient. In fact, contrary to what was known internally, the following was the following was allowed to transpire:

- The Instructions for Use (IFU) supplied with each device stated that the material is not subject to degradation as shown in **Figure 5** below[72] which is directly contrary to what was known[73].

[64]Eth.Mesh.05845592.
[65]Eth.Mesh.15958410.
[66]Eth.Mesh.1283139; Eth.Mesh.12729337; Eth. Mesh.07690752.
[67] Eth.Mesh.15958411.
[68] Eth.Mesh.12831392.
[69] Deposition of Thomas Barbolt, 409:1-13.
[70] Deposition of Thomas Barbolt, 516:21-517:4.
[71] *See* Clave et al. *Polypropylene as a Reinforcement in Pelvic Surgery is not Inert: Comparative Analysis of 100 Explants*. Int. Urogynecol. J. 21:261-270 (2010); Wood, A.J., et al. *Materials Characterization and Histological Analysis of Explanted Polypropylene, PTFE, and PET hernia meshes from an Individual Patient*. J. Mater. Sci. Mater. Med. 24(4): 1113-1122 (2013); Costello, C.R. et al. *Materials Characterization of Explanted Polypropylene Hernia Meshes.* J. Biomed Mater. Res. Part B: Appl. Biomaterials. 83B: 44-49 (2007).
[72]Eth.Mesh.02340568.
[73] Eth.Mesh.12831392.

> Animal studies show that implantation of PROLENE mesh and the absorbable fleece sandwich material made from VICRYL and PDS yarn elicit a minimal inflammatory reaction in tissues, which is transient and is followed by the deposition of a thin fibrous layer of tissue, that can grow through the interstices of the mesh system as the fleece portion is being absorbed, thus incorporating the mesh into adjacent tissue. The PROLENE material is not absorbed, nor is it subject to degradation or weakening by the action of tissue enzymes.

Figure 5: Instructions for Use

In my opinion, prevention of harm or physical injury to the health of people from degradation of the Prolene in the TVT-S was not the focus of risk analysis as it should have been. Unless prevention of hazardous situations is firmly established, the FMEA will turn into an exercise only to meet market requirements rather than ensuring a dynamic process of continual improvement to the product to protect patient safety.

Ethicon internal documentation on the TVT-S device supports my opinion that degradation was a known complication associated with the use of the TVT-S device. Despite Ethicon knowing that *in vivo* degradation was a hazard, this cause of failure was not included in the dFMEA or aFMEA.[74] My opinion is that the design of the TVT-S was inadequate because Ethicon did not accurately represent that there may be dangers associated with the degradation of the TVT-S device, despite Ethicon's own internal documentation to the contrary.

2. Increased stiffness of Laser Cut Mesh

The TVT-S device is offered exclusively with laser cut mesh, not mechanical cut mesh.[75] The laser cut mesh had substantially different physical properties than the mechanically cut mesh, as the laser cut mesh was stiffer. In March 2006, Gene Kammerer presented results regarding elasticity testing of laser cut mesh and mechanically cut mesh which showed that laser cut mesh was less elastic than mechanically cut mesh: MCM [mechanically cut] meshes stretch between 55.8% and 33.4%. The LCM [laser cut] meshes stretch between 39.5% and 32.1%."[76]

Additionally, a December 14, 2004 Ethicon memo found that at 1" of stretch, the laser cut TVT was "about three times stiffer than the machine cut TVT mesh."[77] However, Ethicon decided against conducting clinical testing to establish the safety and effectiveness of the devices affected by using the laser cut mesh.[78] Relying on the performance of a product with different characteristics, such as the mechanically cut mesh, and assuming the new product or change in manufacturing of the material is safe is not consistent with industry norms.

Additionally, Ethicon Key Opinion Leaders ("KOLs") expressed concern that there were no clinical studies to support the LCM mesh: "from a scientific, but also clinical stand point, it is impossible and incorrect to say or assume that Laser Cut would be the same as mechanically cut. Comparative in vivo studies is a necessity to determine the differences. Theoretical calculations

[74] Eth.Mesh.00309351; T-0465 (Exhibit from June 5, 2013 Deposition of Dan Smith).
[75] Eth.Mesh.00309362.
[76] Eth.Mesh.00302181.
[77] Eth.Mesh.01809080.
[78] Eth.Mesh.00167104 (April 18, 2006 Clinical Expert Report for Laser Cut Mesh).

are not enough as evidence."[79] Ethicon documentation has revealed that stiffer meshes may lead to complications in patients.[80] Moreover, published, peer-reviewed clinical literature agrees that stiffer meshes are associated with increased patient complications.[81] Despite Ethicon's knowledge that a mesh that is too stiff can cause painful complications, Ethicon continued to sell this mesh to patients and did not warn of these complications. Ethicon's continued marketing of the TVT-S device with laser cut mesh violated industry standards and practices and jeopardized patient safety.

Additional internal documentation on laser cut mesh supports my opinion that it is a deviation from the standards to leverage the performance of old material (MCM) to new material (MCM). Moreover, Ethicon documentation reveals that Professor Carl Gustaf Nilsson, an Ethicon consultant who has published a study on the TVT Retropubic device,[82] has noted that he "Will not use Laser cut mesh."[83]The Laser Cut Mesh dFMEA notes that if a mesh is too stiff it can cause the following harms: "Harm: Pain, Damage to Urethra, Urethral Impingement, Damage to Bladder."[84] The TVT-S Risk Assessment documents do not appear to mitigate the impact of increased stiffness.

3. Instructions for Use ("IFU") did not warn about all known risks

The design of the TVT-S is in adequate because the product's IFU did not warn of all known risks associated with the TVT-S product. For example, Ethicon internal documentation revealed that Ethicon received complaints of dyspareunia and pelvic pain,[85] however, the TVT-S IFU's Adverse Reactions section does not warn of these complications.[86] Additionally, Ethicon know that the TVT-S would invoke pain with the stiffer (laser cut) mesh, but never warned about these risks. The Laser Cut Mesh dFMEA notes that if a mesh is too stiff it can cause the following harms: "Harm: Pain, Damage to Urethra, Urethral Impingement, Damage to Bladder."[87] However, Ethicon failed to disclose all known risks associated with the TVT-S product in the IFU.

Another example of the TVT-S IFU being inadequate is that is represents complications as "transitory": "Transitory local irritation at the wound site and a transitory foreign body response may occur. This response could result in extrusion, erosion, fistula formation, or inflammation."[88] However, Meng Chen, Ethicon's Associate Medical Director of Worldwide Customer Quality,

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[79] Eth.Mesh.16416002.
[80] Eth.Mesh.02185584; Eth.Mesh.08968369; Eth.Mesh.08969368; Eth.Mesh.04077109; Eth.Mesh.08041930.
[81] *See* Dietz, H.P. et al. Mechanical Properties of Urogynecologic Implant Materials. Int. Urogynecol. J. (2003) 14: 239-243; Moalli, P.A., et al. Tensile Properties of Five Commonly Used Mid-Urethral Slings Relative to the TVT. Int. Urogynecol. J. DOI 10.1007/s00192-007-0499-1. (2007); Okulu, E. et al. Use of Three Types of Synthetic Mesh Material in Sling Surgery: A Prospective Randomized Clinical Trial Evaluating Effectiveness and Complications. Scandanavian J. of Urology. 2013; 47: 217-224;
[82] *See* Nilsson, C.G. et al. *Seventeen Years' Follow-Up of the Tension-free Vaginal Tape Procedure for Female Stress Urinary Incontinence*. Int. Urogynecol. J. DOI 10.1007/s00192-013-2090-2 (2013).
[83] Eth.Mesh.04048515.
[84] Eth.Mesh.01218019 (dFMEA for Laser Cut Mesh); Eth.Mesh.22012565 (Technical File Amendment—Laser Cut Mesh.)
[85] Eth.Mesh.04081189; Eth.Mesh.04081301.
[86] Eth.Mesh.02340568.
[87] Eth.Mesh.01218019 (dFMEA for Laser Cut Mesh); Eth.Mesh.22012565 (Technical File Amendment—Laser Cut Mesh.)
[88] Eth.Mesh.02340568.

noted that these issues are not "transitory" at all.[89] Ethicon's failure to include all of the known complications, and the potential severity of those complications, of the TVT-S device is a violation of industry practices and international standards.

4. Physician Problems Tensioning the TVT-S Device

As early as 2007, Ethicon documentation reveals that physicians who had been implanting the TVT-S device were having difficulty implanting it due to problems with the tensioning.[90] In a March 2007 email, Scott Jones, an Ethicon Division Sales Manager, explained that he had a discussion with Dan Smith "about why the tension with TVT SECUR is perceived to be so different."[91] This email further explained that "some doctors have complained that the TVT SECUR device is placed too tight. In reality, we need to be more comfortable explaining the differences between tensioning TVT SECUR vs. previous TVT slings."[92] Scott Jones also warns that "we obviously need to be cautious not to over-tension the sling…"[93]

In a November 2008 document, Dan Smith notes that some surgeons do not understand the tensioning concept as it relates to the TVT Secur product.[94] Dan Smith noted in this document that "[s]urgeons who did listen to our mesh placement suggestions are today successful with TVT Secur."[95] Dan Smith further notes that "TVT SECUR will NEVER get tighter once placed unlike most other slings to date, because of the short 4 cm of free mesh and the laser cut design!"[96] Smith further notes that "[m]ost surgeons have NO idea as to the dynamics of the sling, nor that TVT (Tension-free Vaginal Tape) is actually not tension free, and it never was!"[97] However, the IFU for the TVT-S device notes that TVT-S is "tension-free."[98]

In a November 2007 email, Ethicon's former Medical Director David Robinson discusses a meeting with Professor Frazer, whose experience with TVT-S led him to express his opinion that "the IFU is fundamentally misleading. Tension-free, tension-less and placement with no tension are complete misnomers."[99] In a November 2, 2007 email, Dr. Aran Maree, Ethicon's Medical Director for Australia and New Zealand, noted that "[i]t is my understanding that some suggestions had come out in the form of (i) increased tension required with this mesh with 'pillowing of peri-urethral tissues required,' (which is quite the opposite of TVT-O recommendations), as well as (ii) new tips and tricks to avoid dislodging the device when removing the inserters and (iii) new tips for minimal dissection when introducing the product. We also discussed the fact that at this time some or all of these suggested changes may not be incorporated into the Instructions for Use or technical training manual."[100] Despite these known concerns with the surgical implantation technique of the TVT-S not reflected in the IFU, Ethicon chose to never update the IFU. Ethicon's

[89] Eth.Mesh.04093125.
[90] Eth.Mesh.00006213.
[91] Id.
[92] Id.
[93] Id.
[94] Eth.Mesh.09911296.
[95] Id.
[96] Id.
[97] Id.
[98] Eth.Mesh.02340568.
[99] Eth.Mesh.00327060.
[100] Eth.Mesh.00312180.

continued marketing of the TVT-S device, despite knowledge of the concerns of physicians who were implanting the device, violated industry standards and practices and jeopardized patient safety.

5. Physician Learning Curve with TVT-S

Ethicon documentation reveals that Ethicon was aware that surgeons were having difficulty obtaining successful results with the TVT-S device. As early as November 2006, Ethicon's former Medical Director, David Robinson noted in an email that surgeons were experiencing a learning curve with the TVT-S device.[101] A March 14, 2007 email sent by Dr. David Robinson to Dr. Axel Arnaud acknowledged that the first human use study taught "that the learning curve is longer than we thought, mesh tensioning is different than kits with sheaths, and that following the IFU is important."[102] During a June 18, 2008 interview, Carl. G. Nilsson, an Ethicon Key Opinion Leader, stated that the learning curve for him with the TVT-S was "100 patients before he was very good with very dry results."[103] Additionally, an August 19, 2007 Ethicon presentation showed that there were several "[m]ain difficulties/complications" with the TVT Secur: "Insertion difficulties, Releasing difficulties, Fixation tips not staying in place, Bladder perforation, Excessive bleeding, Failures – Tensioning."[104]

In November 2007, the decision was made to withdraw the TVT-S product entirely from the market in Australia.[105] Dr. Aran Maree, the Medical Director for Ethicon in Australia emailed Catherine Beath stating "We feel that withdrawing the product from the market here is currently the most appropriate action for Australia. We believe this to be appropriate until we are confident that a modified technique, appropriately documented and tested by way of a clinical study, can be taught to our surgeons and will lead to optimal patient outcomes with this product."[106] In 2008, after the TVT-S product was removed from the market in Australia, Rosalyn Harcourt, a Senior Product Manager, emailed Aran Maree and provided a "summary of the key reasons surgeons do not wish to be re-trained on TVT Secur at this point in time" including "lack of clinical evidence," "steep learning curve," and "IFU versus 'nuances' –very different."[107]

6. Difficulty Removing the TVT-S Device

Ethicon did not identify the difficulty of removing their products, including the TVT-S. There are a number of reasons a permanent implant may need to be removed or replaced. The device could fail to perform its intended function or result in one or more of the harmful situations defined in this section ("Critical Risks Ignored by Ethicon"). Additionally there could be other medical complications that necessitate removal of the device in full or in part.

Evidence from Ethicon's former Medical Director Piet Hinoul supports my opinion that the TVT products, including TVT-S, were difficult to remove. He has acknowledged that "once the

[101] Eth.Mesh.00153967.
[102] Eth.Mesh.03922618.
[103] Eth.Mesh.04048515 (Notably, Nilsson also stated in this interview that he "[w]ill not use Laser-cut mesh!! Does not have the same stretch profile of Mechanical-cut mesh.").
[104] Eth.Mesh.02105223.
[105] *See* Eth.Mesh.00326842; Eth.Mesh.00647410; Eth.Mesh.00832210; Eth.Mesh.02154877.
[106] Eth.Mesh.00326842.
[107] Eth.Mesh.04127331.

TVT is incorporated into the body, if a complication is resulting from the TVT's presence within the body" it "can be very difficult to treat at times because of the fact that it's permanently incorporated into the tissue."[108] Piet Hinoul further testified that "removal of the mesh, because you get tissue ingrowth, can prove to be a challenge."[109] Ethicon Medical Director David Robinson also acknowledged that physicians were difficulty removing the TVT device.[110]

VIII. ETHICON MANAGEMENT DID NOT UPDATE THE TVT DEVICE'S WARNING INFORMATION, DESPITE KNOWLEDGE OF PRODUCT COMPLICATIONS

As I have explained above, Ethicon's management had a responsibility to evaluate and assess product complaints regarding the TVT-S device and then incorporate that information into the design of the device, including the physical design, protective measures and/or changes to the device labeling. There must have been documentation of the response to these complaints. Ethicon documentation and testimony reveals that Ethicon's management were alerted by Meng Chen, Ethicon's Medical Director and Safety Surveillance Director, who testified that she "repeatedly observed" complaints of "dyspareunia" in reports regarding Ethicon's TVT products.[111] Meng Chen acknowledged that "because of the frequency with which" she saw dyspareunia, she "alerted some of [her] superiors at the company and made them aware of that."[112] Ethicon documentation reveals that after reading patient complaints relating to Ethicon's TVT family of products, Meng Chen wrote an email to Ethicon Management, including Mark Yale, the head of Ethicon's Quality Engineering and Risk Management department at that time, in which she stated "[o]ur post-market knowledge with these products are much more than what we have in the IFUs for all three types of TVTs…My reason for bringing this point to you is maybe you may be able to look into it from senior management perspective and to facilitated the IFU updated for all three TVTs, particularly in the area of 'Potential Adverse Reactions.'"[113] Meng Chen testified at her deposition, that since

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108 Deposition of Piet Hinoul, January 13, 2014, 807:3-18 (Q. –once it's been incorporated into the body, you can't simply adjust it. You'd have to actually cut into it and move—and remove part of the tape, correct? A. Sometimes people try to loosen it, but I would just say—I would agree with you, it's not designed to be readjust able post-replacement. Q. Once—I'm sorry. Once the TVT is incorporated into the body, if a complication is resulting from the TVT's presence within the body that can be very difficult to treat at times because of the fact that it's permanently incorporated into the tissue, correct? A. That is correct.") and Deposition of Piet Hinoul, January 13, 2014, 809:11-810:5 (Q.—and then later an infection occurs, there can be difficulty removing the infected mesh, right? A. In that sequence of events, yes. Q. If mesh has been fully integrated and then an erosion occurs, it can be difficult to remove the full amount of the mesh that you want to remove. You may be able to get the part that's exposed into the vagina— A. Right. Q. –but when you want to get deeper into the tissue,that can be difficult, correct? A. Yes. And from personal experience, we would never advocate to take the whole mesh out if it's not necessary to take the whole mesh out.").

109 Deposition of Piet Hinoul, June 27, 2013, 578: 15-22 (Q. If a patient has a complication that is chronic pain or pain with sex or another complication and the mesh is removed, can that be very difficult?.A. Yes. Removal of the mesh, because you get tissue ingrowth, can prove to be a challenge.").

110 Deposition of David Robinson, July 24, 2013, 181:12-18 ("So, physicians within the United States it looks like from these complaints were having difficulty inserting or difficulty removing the device, at least the physicians who were making these complaints.? A. Well, there were complaints of such, yes.").

111 Deposition of Meng Chen, October 29, 2013, 121:13-19; *See* Eth.Mesh. 04081301.

112 Deposition of Meng Chen, October 29, 2013, 121:21-25.

113 Eth.Mesh.04092868; Deposition of Meng Chen, October 29, 2013, 189:13-190:21.

she brought a "medical doctor's perspective" she had a perspective that that senior management may not have.[114] Meng Chen further testified that updating the IFU to a level that reflected the current knowledge of the manufacturers on the potential adverse reactions associated with the TVT products was crucial because this would allow physicians to "conduct a more thorough and more effective preoperative risk-benefit consent."[115] Ethicon management never addressed these issues raised by Meng Chen. Ethicon management's inaction on this issue, as required by the foregoing design standards, fundamentally ignored patient concerns and the safety of this permanently implantable device. As explained in this report, this started from the very beginning of the acquisition of the device, through its early development and after it was released to market. Well-recognized international standards for quality management systems and Ethicon's own internal guidelines were not effectively performed to put patient safety first by effectively planning for and mitigating risk. That is fundamentally part of a safe and effective design. Unfortunately, neither the design standards nor their internal procedures were followed for the TVT-S system.

I reserve the right to supplement or alter my opinions based on the review of additional material or information.

IX. COMPENSATION

The compensation per hour which I expect to be paid for my review, study, and testimony is as follows: $365.00 per hour for review and study, expert report, deposition and trial testimony time.

X. LISTING OF CASES IN WHICH TESTIMONY HAS BEEN GIVEN IN THE LAST FOUR YEARS

1) Arthrex, Inc & Arthrex Manufacturing Inc. v. Parcus Medical, LLC
2) Mullins et al. v. Ethicon

XI. EXHIBITS

1) Anne H. Wilson Curriculum Vitae
2) ISO 14971 Flow Chart
3) Facts and Data Considered

Anne Holland Wilson

Digitally signed by Anne Holland Wilson
DN: cn=Anne Holland Wilson, o=QA Consulting, Inc., ou, email=awilson@qaconsultinginc.com, c=US
Date: 2016.02.01 07:40:50 -06'00'

[114] Deposition of Meng Chen, October, 29, 2013, 191:23-192:2.
[115] Deposition of Meng Chen, October, 29, 2013, 201:20-202:10.